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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,849	04/09/2007	Brian Smith	20750-048US1	2290

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
10/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/576,849	SMITH ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11,13,16,17,19-32 and 48* is/are rejected.

7)☒ Claim(s) *3,12,14,15 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/19/08 & 2/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-32 and 48 are pending in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 25, 26 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The scope of diseases and/or conditions associated with the modulation of the $5HT_{2C}$ receptor cannot be deemed enabled. The terms "disorders of the central nervous system, cardiovascular disorders and gastrointestinal disorders" covers a broad array of different disorders that have different modes of action and different origins. For example the term “disorders of the central nervous system” covers such diverse disorders as Alzheimer's Disease; Parkinson's Disease; ALS and variants such as forms of ALS-PDC; Gerstmann-Straussler-Scheinker Disease (GSS); Pick's Disease; Diffuse Lewy Body Disease; Hallervordon-Spatz disease; progressive familiar myoclonic epilepsy; Corticodentatonigral degeneration; progressive supranuclear palsy (Steele-Richardson-Olszewski);

Huntington's disease; more than a dozen dementias collectively called "frontotemporal dementia and Parkinsonism linked to chromosome 17" (FTDP-17); Tourette's syndrome; Shy-Drager syndrome; Friedrich's ataxia and other spinocerebellar degenerations; Olivopontocerebellar atrophy (OPCA); spasmotic torticollis; Striatonigral degeneration; various types of torsion dystonia; certain spinal muscular atrophies, such as Werdnig-Hoffmann and Wohlfart-Kugelberg-Welander; Hereditary spastic paraplegia, Primary lateral sclerosis; peroneal muscular atrophy (Charcot-Marie-Tooth); Creutzfeldt-Jakob Disease (CJD); Hypertrophic interstitial polyneuropathy (Dejerine-Sottas); retinitis pigmentosa; Leber's Disease; and Hypertrophic interstitial polyneuropathy. These exhibit a very broad range of effects and origins. For example, some give progressive dementia without other prominent neurological signs, such as Alzheimer's disease, whereas other dementias have such signs, such as Diffuse Lewy Body Disease. Some give muscular wasting without sensory changes, e.g. ALS, and some do have the sensory changes such as Werdnig-Hoffmann. Some are abnormalities of posture, movement or speech, such as Striatonigral degeneration, and other are progressive ataxias, such as OPCA. Some are linked to tau mutations, such as Alzheimer's disease and FTDP-17, and other such as Parkinson's clearly do not. Some affect only vision such as retinitis pigmentosa. Even within those that fall into the same category of effects, there are often striking differences. For example, Alzheimer's disease and Pick's disease both give progressive dementia without other prominent neurological signs. But the characteristic Alzheimer's neurofibrillary tangles are not seen in Pick's Disease, which has straight fibrils, as opposed to the paired helical filaments of Alzheimer's

disease. Pick's Disease gives lobal atrophy, not seen in Alzheimer's disease. There are differences in origins, even with what little is known. Thus, among progressive dementias, CJD is definitely caused by an infectious agent; so far as can be determined, this is not so for Huntington's disease. Even among the hereditary disorders, the origins are different. Thus, FTDP-17 comes from chromosome 17, Huntington's disease from 4, and the neurodegenerative disorder that people with Down's syndrome develop later in life is presumably connected in some way to 21.

The great majority of these have no treatment at all, and of those that do, none or virtually none have been treated with such inhibitors as are disclosed here. The great diversity of diseases falling within the "disorders of the central nervous system" category means that it is contrary to medical understanding that any agent (let alone a genus of trillions of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. Further, what little success there has been does not point in this direction. Thus, what very few treatments that the massive research effort on Alzheimer's disease has produced are means of providing Acetylcholinesterase inhibition, unrelated to the mechanism of action in this case.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See In re Ruskin, 148 USPQ 221, Ex parte Jovanovics, 21 1 USPQ 907, MPEP 2164.05(a).

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQZd 1001.

2. Claims 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of "diagnosis, treatment, prevention or alleviation ….. drug and alcohol addiction" cannot be deemed enabled. The notion that a compound could be effective against chemical dependencies in general is contrary to our current understanding of how chemical dependencies operate. There is not, and probably never will be, a pharmacological treatment for "drug addiction" generally. That is because "drug addiction" is not a single disease or cluster of related disorders, but in fact, a collection with relatively little in common. Addiction to barbiturates, alcohol, cocaine, opiates, amphetamines, benzodiazepines, nicotine, etc all involve different parts of the CNS system; different receptors in the body. For example, cocaine binds at the dopamine re-uptake site. Heroin addiction, for example, arises from binding at the opiate receptors, cigarette addiction from some interaction at the nicotinic acid receptors, many tranquilizers involve the benzodiazepine receptor, alcohol involves yet another system, etc. All attempts to find a pharmaceutical to treat chemical addictions generally have thus failed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 2, 4-11, 13, 16, 17, 20, 24-27, 29-32 and 48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8-14, 17-22, 25 and 77 of U.S. Patent No. 6,953,787. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds, compositions and method of use of the compounds of formula I of the instant invention are embraced by the compounds, compositions and method of use of the compounds of U.S. '787 where R^1 is H or C_{1-8} alkyl; R^2 is C_{1-8} alkyl; R^3 is H; Ar is aryl or heteroaryl; Z is S or absent; Y is C_1-C_{10} alkylenyl; and X is S, N or absent.

4. Claims 25-27 and 29-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 13-22, 31-47,

58-67, 73 and 75 of copending Application No. 10/917,979. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of use of the compounds of formula I of the instant invention are embraced by the method of use of the compounds of 10/917,979 where R^1 is H or C_{1-8} alkyl; R^2 is C_{1-8} alkyl; R^3 is H; Ar is aryl or heteroaryl; Z is O, S or absent; Y is C_1-C_{10} alkylenyl; and X is O, S, N or absent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 1, 2, 4-11, 13, 16, 17, 19, 20, 24-27 and 29-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 6, 7 and 9-12 of copending Application No. 11/599,050. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds, compositions and method of use of the compounds of formula I of the instant invention are embraced by the method of use of the compounds of 11/599,050 where R^1 is H or C_{1-8} alkyl; R^2 is C_{1-8} alkyl; R^3 is H; Ar is aryl or heteroaryl; Z is O, S or absent; Y is C_1-C_{10} alkylenyl; and X is O, S, N or absent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 1, 2, 4-11, 16, 17, 19, 20 and 24-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-50, 52-55 and 58-65 of copending Application No. 10/560,953. Although the

conflicting claims are not identical, they are not patentably distinct from each other because the method of use of the compounds of formula I of the instant invention are embraced by the method of use of the compounds of 10/560,953 where R^1 is H or C_{1-8} alkyl; R^2 is C_{1-8} alkyl; R^3 is H; Ar is aryl or heteroaryl; Z is O or absent; Y is C_1-C_{10} alkylenyl; and X is O, N or absent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 1, 2, 4-11, 13, 16, 17, 19-32 and 48 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 and 42 of copending Application No. 10/573,196. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of use of the compounds of formula I of the instant invention are embraced by the method of use of the compounds of 10/573,196 where R^1 is H or C_{1-8} alkyl; R^2 is C_{1-8} alkyl; R^3 is H; Ar is aryl or heteroaryl; Z is O or absent; Y is C_1-C_{10} alkylenyl; and X is O, N or absent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

8. Claims 3, 12, 14, 15 and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. None of the prior art of record

or a search in the pertinent art area teaches the compounds of formula I where Ar-Z-Y-X- is Ar-Z-Y-CO-, phenyl-Z-C_1-C_8 alkylenyl-CO-, phenyl-C_1-C_6 alkylenyl-CONR^7-, phenyl-CONR^7-, phenyl-C_1-C_6 alkylenyl-, pyridyl-C_1-C_6 alkylenyl-, phenyl-methylene or phenyl-ethylene.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624